

*Page 55, line 12 to page 56, line 6, please replace the paragraph with the following:*

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10031398-011802  
The renin-angiotensin system is revealed to play an important role in the progress of cerebrovascular lesions accompanying hypertension. Then, a compound having an AII antagonistic activity (particularly Candesartan cilexetil) can be expected to inhibit cerebral arteriosclerosis and the progress of arteriosclerotic lesions (for example, carotid artery lesions) responsible for ischemic cerebrovascular disorder not only by the vasodilator action but also by the action of improving endothelial cell functions and inhibiting inner membrane thickening (correction of vascular remodeling). Further, reduction in cerebral blood flow and microcirculation in brain are ameliorated by the action of ameliorating the ability for automatic circulation of cerebral circulation, and there are further brought about various actions for protection of brain (nerves), correction of an abnormality in fibrinolytic system, amelioration of blood properties, etc. Thus, the compound is useful for preventing recurrence of cerebrovascular disorder or for ameliorating troubles following cerebrovascular disorder and inhibiting progress thereof.

*Page 57, line 17 to page 58, line 16, please replace the paragraph with the following:*

A4  
It has been revealed that AII have not only a strong vasoconstricting action but also various actions such as proliferating action, inflammation action, oxidizing action, vascular penetrating action, etc., thus playing an important role in the progress of not only hypertension but also cerebrovascular lesions. That is, it is reported that AII induces hypertrophy of cells via expression of oncogenes and growth factors, thickens vascular walls by an increase in production of extracellular substrate, activates a transcriptional factor (NF- $\kappa$ B) to increase expression of a monocyte chemotactic factor (Hernandez-Presa M, et al., Circulation 95, 1532-1541, 1997), and induces production of free radicals from inflammatory cells (Zafari AM, et al., Hypertension 32, 488-495, 1998), thus significantly influencing various organ disorders including cerebrovascular disorder. Candesartan cilexetil not only inhibits these disorders attributable to AII thereby treating hypertension but also exerts actions for prevention of progress of arteriosclerosis, amelioration of vessel remodeling, amelioration of microcirculation, inhibition of edema,

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amelioration of endothelial cell functions (promotion of NO production in endothelial cells), and protection of cells thereby preventing the progress and recurrence of cerebrovascular disorder and ameliorating troubles after cerebrovascular disorder.

*Page 58, line 18 to page 59, line 1, please replace the paragraph with the following:*

as  
Candesartan cilexetil is known to improve insulin sensitivity clinically (Iimura O., et al., Am J Hypertens 8, 353-357, 1995), and can ameliorate various disorders accompanying an abnormality in glucose tolerance, diabetes and a reduction in insulin sensitivity as dangerous factors for recurrence of cerebrovascular disorder thereby preventing the progress and recurrence of cerebrovascular disorder and ameliorating troubles after cerebrovascular disorder.

*Page 59, lines 3 to 12, please replace the paragraph with the following:*

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2025-05-05  
Candesartan cilexetil has actions for anti-inflammation, anti-oxidization, anti-edema, amelioration of microcirculation and improvement of endothelial cell functions as described in the above (2), and can inhibit vasoconstriction and promotion of platelet agglutination caused by various vasoconstrictor such as endothelin and thromboxane induced and enhanced by AII, whereby the penumbra region can be saved by amelioration of blood flow and inhibition of cellular disorders at the acute stage of vascular infarction.

#### IN THE CLAIMS

Please cancel claims 16 and 17 without prejudice.

*Please add the following new claim:*

A7  
18. (New) A method for making a pharmaceutical composition for ameliorating troubles following cerebrovascular disorder or inhibiting progress thereof, which comprises administering an effective amount of a compound having an angiotensin II antagonistic activity, a prodrug thereof, or a salt thereof.